RAB27A gene

RAB27A, member RAS oncogene family

Normal Function

The *RAB27A* gene provides instructions for making a protein that is involved in a process called vesicle trafficking, which moves proteins and other molecules within cells in sac-like structures called vesicles. Although the Rab27a protein is found in cells and tissues throughout the body, it appears to be most critical in pigment-producing cells called melanocytes and in certain immune system cells.

In melanocytes, the Rab27a protein helps transport structures called melanosomes. These structures produce a pigment called melanin, which is the substance that gives skin, hair, and eyes their color (pigmentation). Rab27a interacts with proteins produced from the *MLPH* and *MYO5A* genes to form a complex that transports melanosomes to the outer edges of melanocytes. From there, the melanosomes are transferred to other types of cells, where they provide the pigment needed for normal hair, skin, and eye coloring.

The Rab27a protein also plays an important role in immune system cells called T-lymphocytes. These cells recognize and attack foreign invaders, such as viruses and bacteria, to prevent infection and illness. Specifically, Rab27a is involved in cytotoxic granule exostosis, which is the process by which T-lymphocytes release cell-killing (cytotoxic) compounds to destroy foreign invaders.

Health Conditions Related to Genetic Changes

Griscelli syndrome

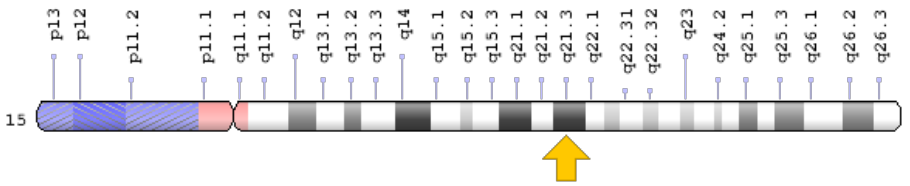
At least 24 mutations in the *RAB27A* gene have been found in people with Griscelli syndrome. These mutations cause a form of the condition designated type 2, which is characterized by unusually light (hypopigmented) skin, silvery-gray hair, and immune system abnormalities. The known mutations either prevent the production of any Rab27a protein or lead to the production of an abnormal or unstable protein that cannot form a complex with the proteins produced from the *MLPH* and *MYO5A* genes. A shortage of functional Rab27a protein impairs the normal transport of melanosomes to the edges of melanocytes. Instead, these structures clump near the center of melanocytes, trapping melanin within these cells and preventing normal pigmentation of skin and hair. A loss of Rab27a function in T-lymphocytes impairs cytotoxic granule exocytosis, making people with Griscelli syndrome type 2 prone to recurrent infections.

Through mechanisms that are not well understood, a shortage of Rab27a in immune system cells also leads to a condition called hemophagocytic lymphohistiocytosis (HLH) in people with Griscelli syndrome type 2. This condition triggers the immune system to produce too many activated T-lymphocytes and other immune cells called macrophages (histiocytes). Overactivity of these cells can damage organs and tissues throughout the body, causing life-threatening complications if the condition is untreated.

Chromosomal Location

Cytogenetic Location: 15q21.3, which is the long (q) arm of chromosome 15 at position 21.3

Molecular Location: base pairs 55,202,966 to 55,291,188 on chromosome 15 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- GS2
- GTP-binding protein Ram
- HsT18676
- rab-27
- RAB27
- RAM
- ras-related protein Rab-27A
- RB27A_HUMAN

Additional Information & Resources

Educational Resources

- Immunobiology (fifth edition, 2001): T Cell-Mediated Cytotoxicity https://www.ncbi.nlm.nih.gov/books/NBK27101/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28RAB27A%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- RAS-ASSOCIATED PROTEIN RAB27A
  http://omim.org/entry/603868

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_RAB27A.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=RAB27A%5Bgene%5D
- HGNC Gene Family: RAB, member RAS oncogene GTPases
  http://www.genenames.org/cgi-bin/genefamilies/set/388
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=9766
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/5873
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